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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/770,885	02/02/2004	Karl Y. Hostetler	UCSD1480-1	1066

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EXAMINER	
MAEWALL, SNIGDHA	
ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

TH

Office Action Summary	Application No.	Applicant(s)	
	10/770,885	HOSTETLER ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

1. Applicant is reminded that the office has not received IDS as of this date.

Claims 1-24 are present in this application and claims 1-24 will be prosecuted on the merits.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "pathological condition". This is a broad genus and does not define metes and bounds of the claim . Applicant is required to recite the specific pathological conditions that are intended to be treated. Similarly "attaching a *moiety* to a therapeutic drug" and treating a disease is a concept. The *"moiety"* should be recited especially in view of applicant's intent to include carboxylates, sulfates and others in the category of "amphiphilic moieties".

Phosphates, carboxylates, sulfates, sulfonates, sulfosuccinates recited in claim 3 are anionic and not amphiphilic.

Claim 4 does not define " C^{α} " which makes the structure indefinite and unclear.

Accordingly the dependent claims 5 and 6 are indefinite.

Claim 16 recites the limitation "derivative of azidothymidine(AZT). The claim is indefinite because it does not define metes and bounds of the claim. The claim limitations under parenthesis and the abbreviations make the claim indefinite. Examiner suggests reciting appropriate and specific compound.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-15 and 22-24 are rejected under 35 U.S.C. 102(a) as being anticipated by Cheng et al. (Feb. 2002) (herein onwards Cheng et al. I). (Investigative Ophthalmology & Visual Science, Feb. 2002, Vol. 43).

Cheng et al. disclose the intraocular drug delivery system using the free crystalline lipid prodrug of ganciclovir, HDP-P-GCV, as a prototype. Cheng et al. discloses a local

intravitreal drug administration for vitrreoretinal diseases, which bypasses the blood-ocular barriers and allows higher intraocular drug levels and avoids many side effects associated with systemic therapy. The intraocular drug delivery may also provide constant and slow release drug. Cheng et al. further disclose that surgical placement and replacement of intravitreal implants can cause significant adverse effects, including vitreous hemorrhage, retinal detachment, and endophthalmitis. Cheng et al. disclose that the intravitreal injection of a long-acting drug preparation would be less invasive than surgery and thus in order to prove such, Cheng et al. have demonstrated in the article that crystalline HDP-P-GCV in the form of 8- to 43-micrometer particles may have utility in treating or preventing HSV retinitis when injected intravitreally as infrequently as once a month or less frequently (see page 515, paragraph, 5 and column 2, first paragraph). The local retinal or lens toxicity observed with high doses may be eliminated, and antiviral duration could even be prolonged by using smaller drug particles, which may provide a better release rate and require less drug to maintain a therapeutic vitreous level with the advantage of a smaller drug depot (see page 521, 4th paragraph and column 2, first paragraph).

6. Claims 1-15 and 22-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Cheng et al. (May 2000).
(Investigative Ophthalmology & Visual Science, May 2000, Vol. 41, No. 6).

Cheng et al. disclose that Cytomegalovirus (CMV) infection of the retina is the

most common infection in acquired immune deficiency syndrome (AIDS) patients. (See page 1523, first paragraph).

Ganciclovir (GCV) was the first drug to be approved for CMV infection in AIDS patients. Ganciclovir is effective in treating CMV retinitis by intravenous administration, but the drug does not eliminate the virus from the retina, requiring long-term suppressive maintenance therapy. Systemic toxicity such as bone marrow suppression was also a problem. The sustained-release GCV implant is effective treatment for CMV retinitis and recurrent CMV retinitis, but complications from surgery such as endophthalmitis and retina detachment are sight threatening. Therefore, in an effort to overcome the disclosed threat, Cheng et al. developed a simple, in-office injectable local therapy that would be effective, minimally toxic, and long-lasting for treatment of CMV retinitis (page 1523, column 2, paragraph 2 and 3).

Cheng et al. further disclose the experimental treatment efficacy of 1-O-hexadecylpropanediol-3-phospho-ganciclovir (HDP-P-GCV (see figure 1 and section under pathologic evaluation of the retinisis, page 1524) and disclose that the antiviral agent, HDP-P-GCV, may be very useful as a local therapy for treating CMV retinitis, HSV retinitis, and other intraocular viral infections in both immunocompromised and immunocompetent individuals. This type of self-assembling liposomal prodrug provides a prototype for intraocular drug delivery and may be applied to the delivery of many currently available drugs for chorioretinal or vitreoretinal diseases (page, 1531, last paragraph).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 16-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over (Cheng et al.) or (Cheng et al. I); (Investigative Ophthalmology & Visual Science, May 2000, Vol. 41, No. 6 and Feb. 2002, Vol. 43) as cited above in view of Unger (US Patent No. 6,120,751).

The teachings of Cheng et al. have been discussed above. Cheng et al. do not exclusively teach various nucleosides, antibody or AZT.

Unger discloses compositions comprising charged lipids, targeting ligands and the use of such compositions in drug delivery, targeted drug delivery, therapeutic imaging and diagnostic imaging as well as their use as contrast agents (abstract). The composition comprises various nucleosides, antibody, polyclonal antibody, fab fragments and AZT (column 45 and 46, lines 67 and 1 and column 48, lines 18-25).

It would have been obvious to the one of ordinary skilled in the art at the time the invention was made to incorporate various therapeutic agents such as various nucleosides as cited above in the formulation of Cheng et al. since Cheng et al. suggest that assembling liposomal prodrug provides a prototype for intraocular drug delivery and may be applied to the delivery of many currently available drugs for chorioretinal or

vitreoretinal diseases and Unger teaches that such a composition comprising nucleosides help in targeted delivery. A skilled artisan would have had a reasonable expectation of success in treating pathological condition of ocular tissue with a composition comprising therapeutic agents such as nucleosides.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Snigdha Maewall

Art Unit 1615

/S. Kishore/

Gollamudi S. Kishore, PhD
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